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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,627	06/03/2005	Mohamed Ghoul	C 2752 PCT/US	5468

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COGNIS CORPORATION
PATENT DEPARTMENT
300 BROOKSIDE AVENUE
AMBLER, PA 19002

EXAMINER

KATAKAM, SUDHAKAR

ART UNIT	PAPER NUMBER
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1621

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,627	GHOUL ET AL.	
	Examiner	Art Unit	
	Sudhakar Katakam	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 June 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>6/3/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Objections

1. Claim 29 is objected to because of the following informalities: the "flavanol" is duplicated in the Markush group of selected flavonoids in the claim. Appropriate correction is required.
2. Claim 36 is objected to because it recites that the enzymatic catalyst is selected from the group consisting of *Cadida antartica etc.*, the members of the Markush group are not enzymaptic catalysts, they are microbial organisms. The enzymatic catalyst is selected from these organisms. Appropriate correction is required.

Specification

3. The disclosure is objected to because of the following informalities: In page 1 of the specification refers to (Fig. 1) at the bottom of the page. There are no figures in this application. This should really be "formula (I)" which is present on the next page. Appropriate correction is required.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 19-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Kontogianni et al** (Eur.J.Lipid Sci.Technol., 2001, 103, 655-660) and **Perrier et al** (US 6,235,294).

Kontogianni et al teach production of flavonoid esters by acylation of flavonoids by fatty acids (C8, C10, C12), catalyzed by immobilized lipase in various solvent systems at 45°C at normal pressure conditions. [See page 655].

Kontogianni et al also teach [see page 656]:

2.2. Enzymatic reactions

In a typical experiment, 50 mg of lipase were added to the reaction mixture, which consisted of 16.5 mM flavonoid, 5 ml solvent and 100 mM fatty acid or fatty acid ester. The solvent-free reaction systems consisted of 50 mg lipase, 16.5 mM flavonoid and 5 ml fatty acid or fatty acid ester (20–31 mM). Incubation was carried out at 45 °C under magnetic stirring, in the presence of 3 Å (3×10^{-10} m) molecular sieves (200 mg). Aliquots were withdrawn at different time intervals and centrifuged for the removal of the enzyme for further analysis.

The water activity of the organic solvents, enzyme preparation and substrates was preset by pre-equilibration for 72 h with the appropriate saturated salt solutions (LiCl, $a_w = 0.11$; MgCl_2 , $a_w = 0.31$; CoCl_2 , $a_w = 0.52$; NaNO_3 , $a_w = 0.69$; KNO_3 , $a_w = 0.87$) as described elsewhere [21]. The water activity of the reaction system was kept constant throughout the reaction [22]. Moreover, in order to study the effect of less than 0.1 water activity, the reaction was carried out in the presence of 3 Å molecular sieves (200 mg).

2.5 Purification of the products

Naringin esters were purified by chromatography on silica gel (230–400 mesh, grade 60). The enzyme was filtered off the reaction mixture and after the evaporation of the solvent, the reaction mixture was dissolved in the elution system of the column. The resulting solution was applied to a 23 ml column. The products were eluted with acetonitrile/methanol/water (8/2/0.3) (v/v/v) and the flow rate was 0.8 ml/min.

3.1 Enzymatic acylation in various reaction media

Several solvents were used as a reaction medium for the esterification of rutin and naringin with fatty acids of long carbon chain. Acetone, THF and *tert*-butanol were chosen for this study, mainly because of their lack of toxicity, even though solubilities of flavonoids in these solvents proved to be rather low. In addition, solvent free systems were tested, with the fatty acid performing the role of the acyl donor and the solvent at the same time.

Kontogianni et al also teach the effect of water activity on esterification reactions. In the figure 2, it has been shown that the high water activity values seem to reduce the flavonoid conversion.

Kontogianni et al also teach that molecular sieves absorb the water formed during the esterification reaction, the presence of this desiccant shifts the equilibrium of the reaction toward the synthesis of esters. [see page 658]:

The differences between the **Kontogianni et al** and instant claims are as follows:

(i) **Kontogianni et al** silent on the water concentration of less than 150 mM to the start of the reaction. However, **Kontogianni et al** represent the water concentration in terms of water activity. Please note, water activity can also be represented in terms of water concentration.

(ii) **Kontogianni et al** fails to teach flavonoids other than rutin and naringin.

With regard to (i) of above, **Kontogianni et al** clearly suggests the effect of water concentration on the esterification reaction. Therefore, a skilled person would be motivated to optimize the process through a routine experimentation to find the suitable water concentration for the reaction process.

With regard to (ii) of above, **Perrier et al** teach the formation of flavonoid esters, in an analogous process, from various flavonoids and acylating agents [col. 4 and 5].

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to use the method of Kontogianni to form other flavonoid

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esters such as those of Perrier et al with a reasonable expectation of success. One would have been motivated to control the water concentration to less than 150 mM and with other flavonoids, because the Kontogianni et al teach the effect of water concentration on the enzymatic formation of flavonoid esters. For the foregoing reasons the instantly claimed process is made obvious.

Conclusion

7. No claim is allowed.
8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhakar Katakam whose telephone number is 571-272-9929. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service

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Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sudhakar Katakam/

Examiner, Art Unit 1621

/YVONNE L. EYLER/

Supervisory Patent Examiner, Art Unit 1621